REMARKS/ARGUMENTS

Claims 1-11 were pending. Claims 2-3 and 5-8 were withdrawn. Claims 1-4 and 9-11 are now pending. Claims 1, 4 and 9-11 were rejected. No claims were merely objected to and no claims were allowed. By entry of the foregoing amendment, claims 1, 4 and 9 are cancelled without prejudice, claims 10 and 11 are amended, and new claims 12 and 13 are added. No new matter is presented.

Supplemental Response

Applicants submit herewith a Declaration under 37 C.F.R. §1.132 by Mrs. Cecilia Bonnafous. Applicants were unable to procure in a timely manner a copy of the article labeled as Exhibit F. Applicants intend to submit a copy of the aforementioned article for Exhibit F in a Supplemental Response. Applicants hope to procure said copy within the next two to three weeks.

Oath/Declaration

The examiner asserts the new oath or declaration filed December 4, 2006 is defective.

Applicants submit herewith an Application Data Sheet in compliance with 37 C.F.R. §1.76 to address the deficiencies in the oath/declaration filed December 4, 2006 and overcome the present objection.

In light of the foregoing, Applicants respectfully request the examiner withdraw the objection to the Oath/Declaration.

Disclosure Informalities

The examiner asserts the recitations of "SEQ ID NO:" in Table VIII at page 31 and Table IX at page 33 are incorrect, and also asserts the "SEQ ID NO:" are missing from Tables I and VII.

Applicants have amended Tables I and VII to insert the missing SEQ ID NOS: and amended Tables VIII and IX to correct the incorrect SEQ ID NOS: recited therein.

In light of the foregoing, Applicants respectfully request the examiner find the disclosure no longer contains informalities.

Claim Objections

The examiner asserts claims 9-11 are objected to because the claims recite peptides of SynB1 and SynB3 without providing the sequence identifier "SEQ ID NO:".

Applicants have cancelled claim 9 without prejudice.

Applicants have amended claim 10 and 11 to provide the sequence identifiers for both SynB1 and SynB3.

In light of the foregoing amendments, Applicants respectfully request the examiner withdraw the objections to claims 9-11.

Rejection under 35 U.S.C. §101

The examiner asserts claims 1 and 4 are rejected under 35 U.S.C. §101.

Applicants have cancelled claims 1 and 4 without prejudice.

In light of the foregoing, Applicants contend the present rejection is now moot.

Rejections under 35 U.S.C. §112, first paragraph

The examiner asserts claims 1 and 4 are rejected under 35 U.S.C. §112, first paragraph.

Applicants have cancelled claims 1 and 4 without prejudice.

In light of the foregoing, Applicants contend the present rejection is now moot.

The examiner asserts claims 9-11 are rejected under 35 U.S.C. §112, first paragraph.

Generally, the examiner asserts the present application does not provide sufficient teaching/guidance as to how the full scope of the claims is enabled.

Applicants respectfully traverse the rejection.

With respect to the factors under *In re Wands*, Applicants' amended claim 10 is directed to the treatment of a CNS disease by administering to a patient suffering from a CNS disease a conjugate comprising an active substance for the CNS disease coupled directly or indirectly by a covalent bond to either the SynB1 or SynB3 peptides. Applicants' amended claim 11 is directed to driving a substance across the Blood Brain Barrier (BBB) to the CNS using a conjugate prepared by coupling directly or indirectly an active substance to either a SynB1 or SynB3 peptide by a covalent bond. The breadth of amended claims 10 and 11 recite both a list of active substances to be coupled and a list of the CNS diseases. Applicants contend the breadth of amended claims 10 and 11 are not too broad so as to encompass unspecified variants regarding the

active substances and the diseases to be diagnosed or treated.

Applicants contend the alleged absence of working examples dealing with human test subjects does not prevent one of ordinary skill in the art from being able to perform the administration step recited in amended claim 10. Applicants refer the examiner to the Declaration under 37 C.F.R. §1.132 submitted by Mrs. Cecilia Bonnafous. Mrs. Bonnafous provides numerous examples in the state-of-the-art indicating mouse models of the CNS are considered the most suitable experimental models comparable to a human's CNS. One of ordinary skill in the art recognizes mouse models are frequently utilized throughout medical research to test the transport, delivery and efficacy of pharmaceutical compositions for treating, e.g., brain cancer, pain and meningitis, in place of actual human CNS models. Applicants also contend the description of the specification-as-filed provides a sufficient amount of direction, guidance and quantity of experimentation necessary to prepare and administer the aforementioned conjugate to drive the substance across the BBB as recited in pending amended claim 11.

With respect to the state of the prior art and relative skill of those in the art, Applicants draw the examiner's attention to the articles referenced in the aforementioned Declaration of Mrs. Cecilia Bonnafous. Applicants contend one of ordinary skill in the art can readily understand how to couple and succeed in coupling an aforementioned active substance directly or indirectly by a covalent bond to one of the aforementioned peptides, that

is, SynB1 or SynB3, and to then administer the conjugate as recited in pending amended claim 10. The aforementioned state-of-the-prior art indicates one of ordinary skill in the art understands how to administer a conjugate of an active substance coupled to vectorized peptides, and administer said conjugate *in vitro* and *in vivo*. The state-of-the-prior art and relative skill of one of ordinary skill in the art is aptly demonstrated in the articles submitted with the aforementioned Declaration.

Mrs. Bonnafous, in her opinion, believes one of ordinary skill in the art can carry out the process of treating a CNS disease by administering a conjugate bonded to an active substance as recited in amended claim 10 given the working examples disclosed in the specification-as-filed taken in conjunction with the state-of-the-prior art and skill level of one of ordinary skill in the art. As Mrs. Bonnafous also indicated in the aforementioned Declaration, in her opinion, one of ordinary skill in the art can carry out the process of driving a substance across the BBB to the CNS as recited in amended claim 11 given the working examples disclosed in the specification-as-filed taken in conjunction with the state-of-the-prior art and skill level of one of ordinary skill in the art.

If however the examiner still contends experimentation is necessary in order to practice Applicants' claimed subject matter, Applicants contend the alleged amount of experimentation asserted by the examiner will not rise to the level of being "undue" as recognized by one of ordinary skill in the art in order to administer the conjugate and treat the CNS disease as recited in pending amended claim

10 or to drive an active substance across the BBB to the CNS as recited in pending amended claim 11.

With regard to the predictability and/or unpredictability of the art, Applicants' expert, Mrs. Cecilia Bonnafous believes the aforementioned state-of-the-prior art and the disclosure of the present application provides sufficient basis to predict one of ordinary skill in the art will be able to treat a CNS disease using the aforementioned conjugate recited in pending amended claim 10 and will be able to drive an active substance across the BBB to the CNS using the aforementioned conjugate recited in pending amended claim 11. The aforementioned conjugates recited in pending amended claim 10 utilize active substances presently used to treat CNS diseases and either the SynB1 or SynB3 peptides, which the inventors of the present application have established as being able to drive an active substance across the BBB in a mouse model. The specification-as-filed provides working examples demonstrating the effectiveness in delivering vectorized peptides across the BBB to the CNS in mouse models, and one of ordinary skill in the art can likewise expect to be able to drive an active substance coupled directly or indirectly to either a SynB1 or SynB3 peptide by a covalent bond across the BBB to the CNS of a human patient based upon the state-of-the-prior art and knowledge and skill level possessed by one of ordinary skill in the art. The aforementioned state-of-the-prior art and knowledge of one of ordinary skill in the art supports the opinion of Mrs. Bonnafous as to the predictable nature of the ability of the aforementioned conjugates to treat various CNS diseases

as recited in pending amended claims 10 and 11.

Applicants contend the amendments to claims 10 and 11 in conjunction with the Declaration under 37 C.F.R. 1.132 of Applicants' expert, Mrs. Cecilia Bonnafous, and the foregoing remarks satisfy the requirements under *In re Wands*.

In light of the foregoing, Applicants respectfully request the examiner withdraw the rejection under 35 U.S.C. 112, first paragraph, and find claims 10-13 are allowable.

Rejections under 35 U.S.C. §112, second paragraph

The examiner asserts claims 1 and 4 are rejected under 35 U.S.C. §112, second paragraph.

Applicants have cancelled claims 1 and 4 without prejudice.

In light of the foregoing, Applicants contend the present rejection is now moot.

The examiner asserts claims 9-11 are rejected under 35 U.S.C. §112, second paragraph.

The examiner asserts claims 9-11 are indefinite because the claims allegedly lack essential steps in the process.

Applicants have cancelled claim 9 without prejudice.

Applicants' amended claim 10 recites the following:

> 10. A method for treatment of a Central Nervous System (CNS) disease, comprising administering to a patient suffering from a disease of the CNS a conjugate comprising an active substance for treatment of said disease of the CNS coupled directly or indirectly by a covalent bond to one of the following peptides: SynB1 (SEQ ID NO: 11)

or SynB3 (SEQ ID NO: 12); and treating said disease of the CNS, wherein said active substance is an active chemical molecules, and wherein said disease of the CNS is selected from the group consisting of brain cancer, pain and meningitis.

Applicants' amended claim 11 recites the following:

11. A method for driving a substance across the Blood Brain Barrier (BBB) to the Central Nervous System (CNS), comprising:

preparing a conjugate comprising an active substance coupled directly or indirectly by a covalent bond to one of the following peptides: SynB1 (SEQ ID NO: 11) or SynB3 (SEQ ID NO: 12), wherein said active substance is an active chemical molecules;

administering said conjugate to a patient; and

driving one of the following peptides: SynB1 (SEQ ID NO: 11) or SynB3 (SEQ ID NO: 12) across the BBB to the CNS.

The examiner contends claims 10 and 11 are missing steps such as the effective amount of the conjugate being administered, the outcome of the treatment, the clarity as to how the CNS disease is being diagnosed using the conjugate, and identifying the endpoint of the treatment.

Applicants' amended claim 10 recites the conjugate is being administered in an amount sufficient to treat the CNS disease(s) recited therein. With respect to the outcome and endpoint of the treatment, Applicants refer to the aforementioned Declaration of Applicants' expert, Mrs. Cecilia Bonnafous. Mrs. Bonnafous opines Applicants' disclosure in combination with the state of the prior art provides one of ordinary skill in the art the requisite knowledge in order to practice Applicants' claimed method. Mrs. Bonnafous cites several articles supporting the

contention that Applicants' working examples directed to the administration of vectorized peptides to mouse models provides a sufficient level of knowledge to one of ordinary skill in the art in order to practice the method of Applicants' amended claim 10. Applicants' working examples combined with the state of the prior art and knowledge of one of ordinary skill in the art provide the basis for recognizing the outcome of the treatment as well as identifying the endpoint of the treatment.

Applicants' amended claim 11 recites the conjugate is being administered in an amount sufficient to drive a peptide, e.g., SynB1 or SynB3, across the BBB to the CNS. The desired outcome is driving the conjugate across the BBB to the CNS. And, the endpoint of the treatment is driving the conjugate across the BBB to the CNS. Applicants contend the amendments to claim 11 satisfy the alleged missing steps identified by the examiner.

For at least these reasons, Applicants contend amended claims 10 and 11 contain the allegedly lacking essential process steps identified by the examiner.

In light of the foregoing, Applicants respectfully request the examiner withdraw the rejection under 35 U.S.C. §112, second paragraph, and find claims 10-13 are allowable.

CONCLUSION

In light of the foregoing, it is submitted that all of the claims as pending patentably define over the art of record and an early indication of same is respectfully requested.

An earnest and thorough attempt has been made by the undersigned to resolve the outstanding issues in this case and place same in condition for allowance. If the Examiner has any questions or feels that a telephone or personal interview would be helpful in resolving any outstanding issues which remain in this application after consideration of this amendment, the Examiner is courteously invited to telephone the undersigned and the same would be gratefully appreciated.

It is submitted that the claims as amended herein patentably define over the art relied on by the Examiner and early allowance of same is courteously solicited.

If any fees are required in connection with this case, it is respectfully requested that they be charged to Deposit Account No. 02-0184.

Respectfully submitted,
PHILIPPE CLAIR ET AL.

By /Ross J. Christie #47,492/
Ross J. Christie
Attorney for Applicants
Reg. No.: 47,492

Telephone: 203-777-6628 x.116
Telefax: 203-865-0297

Date: August 28, 2007